Serial No.: 09/334,969 Group Art Unit: 1644 Examiner: M. DiBrino



## MARKED COPY OF AMENDED CLAIMS

SERIAL NO. 09/334,969 Filed June 17, 1999 July 17, 2001

- 1. (Amended) A synthetic multivalent T-cell receptor (TCR) complex for binding to a MHC-peptide complex, which TCR comprises a plurality of T-cell receptors specific for the MHC-peptide complex, wherein each TCR in the complex is a refolded recombinant TCR which comprises:
  - i) a recombinant TCR α or γ chain extracellular domain having a first
    C-terminal dimerization peptide which is heterologous to the α or γ chain; and
  - ii) a recombinant TCR  $\beta$  or  $\delta$  chain extracellular domain having a second C-terminal dimerization peptide which is specifically heterodimerized with the first dimerization peptide to form a heterodimerization domain,

wherein a disulfide bond present in native TCRs between the  $\alpha$  and  $\beta$  or  $\gamma$  and  $\delta$  chains adjacent to the cytoplasmic domain is absent from the recombinant TCR.

- 7. (Amended) The TCR complex according to claim 1, wherein the linker molecule is a multivalent attachment molecule such as avidin, streptavidin, or extravidin.
- 8. (Amended) The TCR complex according to claim 7, wherein at least one of the TCR chains  $\alpha$  or  $\beta$  is derived from a fusion protein comprising an amino acid sequence encoding a protein tag recognition sequence for a modifying enzyme such as biotin.
- 10. (Amended) The TCR complex according to claim 1, comprising a <u>multimerized</u> multimerised recombinant T-cell receptor heterodimer having enhanced binding capability compared to a non-multimeric T-cell receptor heterodimer.
- 11. (Amended) A multivalent TCR complex comprising a <u>multimerized</u> multimerised recombinant TCR heterodimer having enhanced binding capability compared to a non-

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multimeric TCR heterodimer, wherein each TCR in the complex is a refolded recombinant TCR which comprises:

i) a recombinant TCR α or γ chain extracellular domain having a first
 C-terminal dimerization peptide which is heterologous to the α or γ chain; and
 ii) a recombinant TCR β or δ chain extracellular domain having a second C-

with the first dimerization peptide to form a heterodimerization domain.

wherein a disulfide bond present in native TCRs between the  $\alpha$  and  $\beta$  or  $\gamma$  and  $\delta$  chains adjacent to the cytoplasmic domain, is absent from the recombinant TCR.

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- 14. (Amended) The TCR complex according to claim 112 or claim 13, wherein the heterodimerization heterodimerisation domain is a coiled coil domain.
- 15. (Amended) The TCR complex according to claim 14, wherein the <u>dimerization</u> dimerization peptides are c-jun and c-fos <u>dimerization</u> dimerization peptides.
- 16. (Amended) The TCR complex according to claim [12] 11, comprising a flexible linker located between the T cell receptor chains and the heterodimerization peptides.
- 22. (Amended) The TCR complex according to claim 20 or claim 21, wherein the T-cell receptors are attached to the vesicle via <u>derivatized</u> derivatised lipid components of the vesicle.
- 23. (Amended) The TCR complex according to claim 19 or claim 20, wherein the T cell receptors are embedded in the lipid bilayer.

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- 24. (Amended) The TCR complex according to claim 1, wherein the TCRs are attached to a solid structure particle.
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- 33. (New) The TCR complex according to claim 1, wherein the hetereodimerization domain is a coiled coil domain.
- 34. (New) The TCR complex according to claim 33, wherein the dimerization peptides are c-jun and c-fos dimerization peptides.
- 35. (New) The TCR complex according to claim 1, comprising a flexible linker located between the T cell receptor chains and the heterodimerization peptides.

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